



SEQUENCE LISTING

<110> YON, Jeff
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MASURE, Stefan Leo Jozef

<120> Novel BACE Proteins, Nucleic Acid Molecules Therefor, Novel
Crystal Structure of Novel BACE Proteins, and Methods for Making
and Using

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<141> 2004-01-21

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Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg
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Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr
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His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro
165 170 175

Leu Gln Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile
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Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro
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Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile
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215

220

Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys
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<220>

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cgctactacc	agaggcagct	gtccagcaca	taccgagacc	tacggaaggg	tgtgtatgtg	480
ccctacaccc	agggcaagt	ggaaggagag	ctgggcaccg	acctggtaag	catcccccat	540
ggacctcaag	tcactgtgcg	tgccaacatt	gctgccatca	ctgaatcaga	caagttcttc	600
atccaaggct	ccaactggga	aggcatcctg	gggctggcct	atgctgagat	tgccaggcct	660
gacgactccc	tggagccttt	ctttgactct	ctggtaaagc	agaccacgt	tccaacctc	720
ttctccctgc	agctttgtgg	tgctggcttc	cctctccaac	agtctgaagt	gctggcctct	780
gtcggaggga	gcatgatcat	tggaggatc	gaccactcgc	tgtacacagg	cagtctctgg	840
tatacaccca	tccgacgaga	gtggtattat	gaggatgatca	ttgtgagagt	ggagatcaat	900
ggacaggatc	tgaatatgga	ctgcaaggag	tacaactatg	acaagagcat	tgtggacagt	960
ggcaccacca	accttcgttt	gcccagaaga	gtgtttgaag	ctgcagtcaa	atccatcaag	1020

Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
 20 25 30
 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
 35 40 45
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
 50 55 60
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
 65 70 75 80
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
 85 90 95
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
 100 105 110
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
 115 120 125
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
 130 135 140
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
 145 150 155 160
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
 165 170 175
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp
 180 185 190
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
 195 200 205
 Asn Leu Phe Ser Leu His Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
 210 215 220
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
 225 230 235 240
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
 245 250 255
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
 260 265 270

Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
 275 280 285
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
 290 295 300
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
 305 310 315 320
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
 325 330 335
 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
 340 345 350
 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
 355 360 365
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
 370 375 380
 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
 385 390 395 400
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
 405 410 415
 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
 420 425 430
 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
 435 440 445
 Gln Thr Asp Glu Ser
 450

<210> 68
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 <212> PRT
 <213> Homo sapiens

<400> 68

His His His His His
 1 5

<210> 69
 <211> 461
 <212> PRT
 <213> Homo sapiens

<400> 69

Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg
1 5 10 15

Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly
20 25 30

Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu
35 40 45

Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala
50 55 60

Pro His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr
65 70 75 80

Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys
85 90 95

Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro
100 105 110

Asn Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys
115 120 125

Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr
130 135 140

Ala Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser
145 150 155 160

Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys
165 170 175

Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly
180 185 190

Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser
195 200 205

Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile
210 215 220

Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu
225 230 235 240

Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg

	245		250		255
Leu	Pro	Lys	Lys 260	Val	Phe
				Glu	Ala
				Ala 265	Val
				Lys	Ser
				Ile	Lys
					Ala
					Ala
Ser	Ser	Thr 275	Glu	Lys	Phe
				Pro	Asp
				Asp 280	Gly
				Phe	Trp
				Leu	Gly
					285
				Glu	Gln
					Leu
Val	Cys 290	Trp	Gln	Ala	Gly
				Thr	Thr
				295	Pro
				Trp	Asn
					Ile
					300
				Phe	Pro
				Val	Ile
Ser	Leu	Tyr	Leu	Met	Gly
305					310
				Glu	Val
				Thr	Asn
					Gln
					315
				Ser	Phe
				Arg	Ile
					320
Ile	Leu	Pro	Gln	Gln	Tyr
				325	Leu
				Arg	Pro
				Val	Glu
				330	Asp
				Val	Ala
					335
				Thr	Ser
Gln	Asp	Asp	Cys	Tyr	Lys
			340		Phe
				Ala	Ile
				345	Ser
				Gln	Ser
					Ser
					350
				Thr	Gly
					Thr
Val	Met	Gly	Ala	Val	Ile
		355			Met
				Glu	Gly
				360	Phe
				Tyr	Val
					365
				Val	Phe
					Asp
					Arg
Ala	Arg	Lys	Arg	Ile	Gly
370					375
				Ala	Val
				Ser	Ala
					Cys
					380
				His	Val
				His	Asp
Glu	Phe	Arg	Thr	Ala	Ala
385				390	Val
				Glu	Gly
				Pro	Phe
					395
				Val	Thr
					Leu
					Asp
					Met
					400
Glu	Asp	Cys	Gly	Tyr	Asn
			405		Ile
				Pro	Gln
					Thr
					410
				Asp	Glu
					Ser
					Thr
					Leu
					Met
					415
Thr	Ile	Ala	Tyr	Val	Met
		420			Ala
				Ala	Ile
				425	Cys
					Ala
					Leu
					Phe
					Met
					430
					Leu
					Pro
Leu	Cys	Leu	Met	Val	Cys
	435				Gln
					Trp
					440
				Arg	Cys
					Leu
					Arg
					Cys
					445
					Leu
					Arg
					Gln
Gln	His	Asp	Asp	Phe	Ala
	450				Asp
					455
				Asp	Ile
					Ser
					Leu
					Leu
					460
					Lys

<210> 70
 <211> 408
 <212> PRT
 <213> Homo sapiens

<400> 70

Glu	Thr	Asp	Glu	Glu	Pro	Glu	Glu	Pro	Gly	Arg	Arg	Gly	Ser	Phe	Val
1			5						10					15	

Glu Met Val Asp₂₀ Asn Leu Arg Gly Lys₂₅ Ser Gly Gln Gly Tyr Tyr Val
 Glu Met Thr₃₅ Val Gly Ser Pro Pro₄₀ Gln Thr Leu Asn Ile₄₅ Leu Val Asp
 Thr Gly₅₀ Ser Ser Asn Phe Ala₅₅ Val Gly Ala Ala Pro₆₀ His Pro Phe Leu
 His Arg Tyr Tyr Gln Arg₇₀ Gln Leu Ser Ser Thr₇₅ Tyr Arg Asp Leu Arg₈₀
 Lys Gly Val Tyr₈₅ Val Pro Tyr Thr Gln Gly₉₀ Lys Trp Glu Gly₉₅ Glu Leu
 Gly Thr Asp Leu₁₀₀ Val Ser Ile Pro His₁₀₅ Gly Pro Gln Val Thr₁₁₀ Val Arg
 Ala Asn Ile₁₁₅ Ala Ala Ile Thr Glu₁₂₀ Ser Asp Lys Phe Phe₁₂₅ Ile Gln Gly
 Ser Asn Trp Glu Gly Ile Leu₁₃₅ Gly Leu Ala Tyr Ala₁₄₀ Glu Ile Ala Arg
 Pro Asp Asp Ser Leu Glu₁₅₀ Pro Phe Phe Asp Ser₁₅₅ Leu Val Lys Gln Thr₁₆₀
 His Val Pro Asn Leu₁₆₅ Phe Ser Leu Gln Leu₁₇₀ Cys Gly Ala Gly Phe₁₇₅ Pro
 Leu Gln Gln Ser₁₈₀ Glu Val Leu Ala Ser₁₈₅ Val Gly Gly Ser Met₁₉₀ Ile Ile
 Gly Gly Ile₁₉₅ Asp His Ser Leu Tyr₂₀₀ Thr Gly Ser Leu Trp₂₀₅ Tyr Thr Pro
 Ile Arg Arg Glu Trp Tyr Tyr₂₁₅ Glu Val Ile Ile Val₂₂₀ Arg Val Glu Ile
 Asn Gly Gln Asp Leu Lys₂₃₀ Met Asp Cys Lys Glu₂₃₅ Tyr Asn Tyr Asp Lys₂₄₀
 Ser Ile Val Asp Ser₂₄₅ Gly Thr Thr Asn Leu₂₅₀ Arg Leu Pro Lys Lys₂₅₅ Val
 Phe Glu Ala Ala₂₆₀ Val Lys Ser Ile Lys₂₆₅ Ala Ala Ser Ser Thr₂₇₀ Glu Lys

Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala
275 280 285

Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met
290 295 300

Gly Glu Val Thr Gln Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln
305 310 315 320

Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr
325 330 335

Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val
340 345 350

Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile
355 360 365

Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala
370 375 380

Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr
385 390 395 400

Asn Ile Pro Gln Thr Asp Glu Ser
405

<210> 71
<211> 5
<212> PRT
<213> Homo sapiens

<400> 71

His His His His His
1 5

<210> 72
<211> 459
<212> PRT
<213> Homo sapiens

<400> 72

Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val
1 5 10 15

Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
20 25 30

Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
 35 40 45
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
 50 55 60
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
 65 70 75 80
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
 85 90 95
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
 100 105 110
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
 115 120 125
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
 130 135 140
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
 145 150 155 160
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
 165 170 175
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp
 180 185 190
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
 195 200 205
 Asn Leu Phe Ser Leu His Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
 210 215 220
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
 225 230 235 240
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
 245 250 255
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
 260 265 270
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
 275 280 285

Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
 290 295 300
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
 305 310 315 320
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
 325 330 335
 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
 340 345 350
 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
 355 360 365
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
 370 375 380
 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
 385 390 395 400
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
 405 410 415
 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
 420 425 430
 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
 435 440 445
 Gln Thr Asp Glu Ser His His His His His
 450 455